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deprotected chemical functional group until at least two separate oligonucleotides of desired length are formed on the substrate surface wherein during said selective deprotection steps, an electric potential is applied to one or more selected electrodes sufficient to generate electrochemical reagents at the selected electrodes capable of deprotecting the chemical functional groups on said proximate molecules or nucleic acids.

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(Amended) A method for electrochemical placement of a material at a specific location on a substrate, which comprises the steps of:

providing a substrate having at its surface at least one electrode that is proximate to at least one molecule that is reactive with an electrochemically generated reagent,

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providing a buffering or a scavenging solution in contact with the substrate at a concentration from about 1 mM to about 100 mM;

applying a potential to the electrode sufficient to generate electrochemical reagents capable of reacting to the at least one molecule proximate to the electrode, and  
producing a chemical reaction thereby.

#### REMARKS

Claims 1, 3-9, 11-16, 22-41 and 44-47 are pending in the present application. Applicant respectfully requests reconsideration of the above-identified patent application in view of the foregoing amendment and following remarks. Applicant has amended claims 16, 41 and 47 to add the clause "providing a buffering or a scavenging solution in contact with the substrate at a concentration from about 1 mM to about 100 mM." Support for this clause can be found in the parent patent (6,093,302) at column 21 lines 51-65. No new matter has been added. Entry of the foregoing amendment is respectfully requested.

#### Objection

Claim 39 was objected to as based upon a canceled claim (17). Claim 39 was amended so that it now depends from claim 16.

#### 35 U.S.C. §103 Rejections

Claims 1,3-9, 11-16, 22-41, 44 and 47 were rejected under 35 U.S.C. §103(a) as unpatentable in view of Heller (U.S. Patent 5,929,208) in view of Southern (U.S. Patent 5,667,667). The Examiner contends that Heller discloses the following elements: (1) "electrophoretic synthesis of polymers" (2) "providing a plurality of reaction locations on a substrate" (3) "each reaction location being individually

electronically addressable and proximate to at least one molecule bearing one protected chemical functional group" (4) "applying potential to said electrode sufficient to generate reagents" (5) "removing the protected group" and (6) "coupling a reagent to the deprotected group to form a monomer." With regards to Southern, the Examiner contends that Southern discloses the following: (1) "a method for electrochemical placement of a material at a specific location on a substrate array" (2) a method comprising the steps (a) "providing a substrate having at its surface at least one electrode that is proximate to at least one molecule bearing at least one protected chemical function group" (a quote of the first element of claim 1 but citing column 10 lines 52-57 of Southern); (b) "applying a potential to said electrode sufficient to generate electrochemical reagents capable of deprotecting at least one of the protected chemical functional groups of said molecule" (a quote of the second element of claim 1 but citing Southern column 10 lines 59-61 and column 6 lines 47-49); and (c) "producing a chemical reaction thereby and bonding the deprotected chemical functional group with a monomer or a pre-formed molecule" (a quote of the third and last element of claim 1 citing Southern column 10, lines 62-64). Applicant respectfully traverses this rejection because (1) the two references cited do not teach that which the Examiner alleges they teach to a person of ordinary skill in the art, (2) because there is no required disclosure or suggestion in either reference to suggest their combination, and (3) because the combined disclosures of Heller and Southern, if they could be properly combined, do not disclose or suggest the claimed invention.

1. Neither Heller or Southern teach or suggest those elements that the Examiner alleges they disclose. As shown above, the Examiner alleges that Heller and Southern teach various elements of the claimed invention using the exact words of elements of the claimed invention and citing sections of the references where these elements are alleged to be disclosed. Applicant respectfully disagrees with this characterization of both Heller and Southern in the words of the claimed invention.

With regard to Heller, the Examiner cites column 39 lines 35-48 and column 40 lines 1-35 (essentially Heller claims 6-17) for the elements (1) "electrophoretic synthesis of polymers" (2) "providing a plurality of reaction locations on a substrate" (3) "each reaction location being individually electronically addressable and proximate to at least one molecule bearing one protected chemical functional group" (4) "applying potential to said electrode sufficient to generate reagents" (5) "removing the protected group" and (6) "coupling a reagent to the deprotected group to form a monomer." Heller claim 6 is the independent claim with claims 7-17 depending upon claim 6 (directly or indirectly). Looking at Heller claim 6, it provides for a "**charged** reactant on the **device adjacent** the locations" (emphasis added). The Heller process, as disclosed in claim 6, requires that the electrodes attract a charged reactant. This is stated "biasing those locations **attractive** to the **charged** reactant." (emphasis added) The Heller process uses **charge attraction** to move a charged reactant to a location "adjacent" to

the biased electrodes. The two "locations" of electrodes in Heller are either "attractive" (column 39 lines 44-46) or "repulsive" (column 39 lines 47-49) "to the charged reactant."

Applicant submits that a reference must be read for all that it teaches, including that which it teaches away from the present invention. Heller clearly teaches away from the present invention by teaching electrodes that function to attract or repel charged reactants. Heller does not teach or suggest, as the Examiner contends, that (3) there are molecules (reactants) having a protected chemical functional group, that (4) the potential applied to electrodes generates chemical reactants, or (5) that a protected group is removed. Therefore, Heller, like many prior art references<sup>1</sup>, discloses that certain semiconductor devices are generated that have addressable electrodes. Accordingly, at best, Heller provides a disclosure of an addressable electrode but does not disclose or suggest any of the elements of claim 1.

With regard to Southern, the Examiner has essentially pointed to claim 6 as disclosing the second and third elements of the present claim 1 (as amended). However, Southern claim 6 differs from the present invention in the relationship between the "surface" and the "electrode" which Southern sets forth in rows.<sup>2</sup> As noted above, a reference must be considered for all it discloses, including those parts that teach away from the claimed invention. Thus, Southern teaches surfaces and regions of the surface that are separate and distinct from the electrode. Using the terminology of the present claim 1, the "surface" term has at least one electrode. In contrast, the "surface" of Southern claim 6 is described as "carrying a protecting group" (column 10 line 55) and the electrode is located at "adjacent regions of the surface" (column 10 line 57). This vast difference in design and methods is best illustrated by comparing Southern Figure 2c and 2d (where the surface, denoted 18, is separate from the electrodes, denoted 16), with Figures 1 or 2 of the present specification which show the "surface" and the electrode to be the same. Therefore, Southern does not disclose or suggest "providing a substrate having at its surface at least one electrode that is proximate to at least one molecule bearing at least one protected chemical function group" in contrast to the Examiner's allegations. Moreover, the other claim elements of the present invention do not make sense in view of this different use of the term "surface" in Southern.

2. In order to properly combine the Heller and Southern references there must be some suggestion in the references to suggest their combination. The suggestion for such a combination cannot be gleaned from the present specification, nor can the claims be used as a template to piece together a facsimile of the claimed invention using pieces of the prior art. The Heller reference relates to attracting or repelling charged reactants to electrodes or away from electrodes. Southern, by contrast, relates to "chemically modify[ing] a substance on the [a] surface adjacent the electrode." (See e.g., Southern

<sup>1</sup> It should be noted that Hollis et al. U.S. Patent 5,653,939 is duplicative of Heller, is 35 U.S.C. §102(e) prior art to Heller, and renders Heller anticipated. Hollis also discloses separately addressable electrodes and attraction and repelling of charged reactants for the same purposes as Heller.

<sup>2</sup> see Southern cited section column 6 lines 45-55 for the whole context of the Southern disclosure.

abstract). Therefore, the methods are totally different and the steps of Southern are not suggested to be used with electrode attraction/repulsion of charged reactants.

Moreover, the physical containment aspect of Southern is modified by physical structure, such as depth of liquid between the surface and the electrode (column 3 lines 4-19) and "electrical caging" of ions (column 3 lines 27-42). This is in direct contrast to Heller's physical attraction or repulsion of charged reactants (in contrast with Southern's protected reactants). Therefore, there is no suggestion in Southern to use electrodes for attraction or repulsion and there is no suggestion in Heller to create electrochemical ions<sup>3</sup>. Accordingly, no requisite suggestion for combination can be found in either Heller or Southern. In view of the inability to combine Heller and Southern, the present rejection is improper. Applicant respectfully requests the withdrawal of the unpatentability rejection over Heller in view of Southern.

3. The combined disclosure, even if such a combination could properly be made, does not teach the claimed invention. As noted above, Heller teaches away from the claimed invention in view of permeation layers and attraction or repulsion of charged reactants. As Heller is the primary reference, it only adds that semiconductors can be made with addressable electrodes. However, a reference must be considered for all that it teaches, including the parts that teach away from the claimed invention. Therefore, the combined teachings include those sections of Heller that indicate that a permeation layer is needed to "avoid[s] adverse electrochemical effects to the binding entities, reactants, and analytes." (Heller, column 13 lines 42-44) The present invention, by contrast, uses (not avoids) "electrochemical effects" to affect a regional pH change to remove a "protected chemical functional group." Therefore, Heller teaches away from the claimed invention and any combined disclosure with Heller must also teach away from the claimed invention.

In addition, Southern teaches away from the claim invention with regard to its notion of "surface" being "adjacent" to electrodes. The present invention, by contrast, provides "a substrate having at its **surface** at least one electrode that is **proximate** to at least one molecule bearing at least one protected chemical functional group." Therefore, the Southern "surface" teaches away from the claimed "surface" of the present invention. Accordingly, both Heller and Southern teach away from the claimed invention

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<sup>3</sup> In fact, Heller teaches away from generation of electrochemical ions to affect attraction or repulsion of charged reactants through the use of a permeation layer separating the binding layer from the electrode. ("a functional device requires some fraction (~5% to 25%) of the actual metal micro-electrode surface to remain accessible to solvent (H<sub>2</sub>O) molecules, and to allow the diffusion of counterions (e.g., Na<sup>+</sup> and Cl<sup>-</sup>) and electrolysis gases (e.g., O<sub>2</sub> and H<sub>2</sub>) to occur. . . . The permeation layer keeps the active micro-electrode surface physically distinct from the binding entity layer of the micro-location. In terms of the primary device function, this design allows the electrolysis reactions required for electrophoretic transport to occur on micro-electrode surface, but avoids adverse electrochemical effects to the binding entities, reactants and analytes." (Heller, column 13 lines 27-44) Therefore, Heller teaches the addition of a permeation layer to prevent electrochemically-generated reagents (i.e., H<sup>+</sup> and OH<sup>-</sup>) from water or pH shifts from reaching the "reaction layer" where Heller's "charged reactants" supposedly bind. Southern, by contrast, uses the electrochemically-generated reagents to change pH and deprotect molecules. Therefore, Heller teaches away from Southern and Southern teaches away from Heller.

and even if the disclosures could be combined, the combined disclosures also teach away from the claimed invention as the teaching away from parts of both Heller and Southern relate to different elements of the claimed invention.

In view of any of the foregoing three reasons or in view of all three reasons, the claimed invention is patentable (1) over Heller **in view of** Southern, or (2) over Heller **and** Southern, or (3) over Heller **or** over Southern.

With regard to claims 16 and 41, the foregoing remarks renders the repeating steps element moot. Moreover, the amendment to claims 16 and 41 further obviates this rejection.

With regard to claims 45 and 46, Southern claim 9 (*i.e.*, column 11 lines 7-9) discloses a counter electrode and not a getter structure. Southern's counter electrodes are illustrated as adjacent rows in Figure 2 (particularly Figure 2c). The present specification getter structure uses this term according to its art-accepted meaning and illustrates a getter structure in Figures 31, 35 and 36 and accompanying text.

#### CONCLUSION

Applicants submit that the claims are now in condition for allowance and earnestly seek rapid advancement as such. Should any questions arise in connection with this submission which may be resolved by a telephonic interview, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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